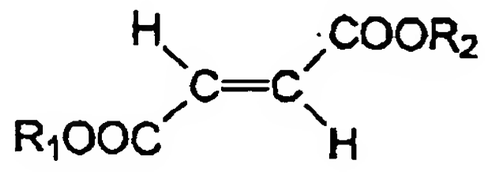
Claims

1. The use of fumaric acid derivatives selected from the group consisting of dialkyl fumarates, monoalkyl hydrogen fumarates, fumaric acid monoalkyl ester salts, fumaric acid monoamides, monoamido fumaric acid salts, fumaric acid diamides, monoalkyl monoamido fumarates, carbocyclic and oxacarbocyclic oligomers of these compounds and mixtures of the foregoing for preparing a drug for the treatment or prevention of cardiac insufficiency, particularly left ventricular insufficiency, myocardial infarct and angina pectoris.

2. The use of fumaric acid derivatives selected from the group consisting of dialkyl fumarates, monoalkyl hydrogen fumarates, fumaric acid monoalkyl ester salts, fumaric acid monoamides, monoamido fumaric acid salts, fumaric acid diamides, monoalkyl monoamido fumarates, carbocyclic and oxacarbocyclic oligomers of these compounds and mixtures of the foregoing for preparing a drug for the treatment of asthma and chronic obstructive pulmonary diseases in general, especially asthma caused by allergies, infections, analgesics, job conditions or physical effort, mixed forms of asthma, or asthma cardiale.

3. The use according to claim 2 in combination with a glucocorticoid, preferably selected from the group consisting of dexamethasone, cortisone, hydrocortisone, prednisolone, prednisone, methylprednisolone, fluocortolone, triamcinolone, beclomethasone, budenoside, flunisonide, fluticasone, betamethasone, and pharmaceutically acceptable salts and derivatives thereof.

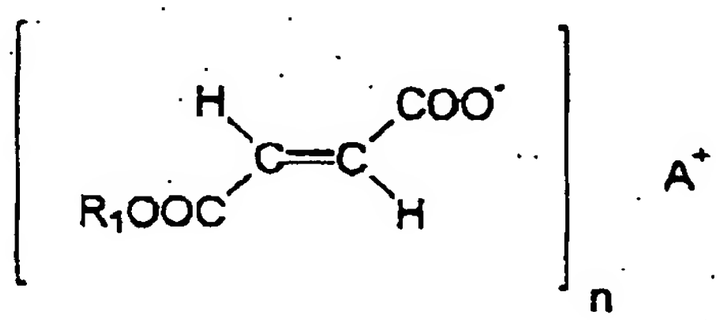
4. The use according to claim 1, 2 or 3 wherein the fumaric acid derivative is selected from one or more fumaric acid dialkyl esters of the formula I



wherein R_1 and R_2 which may be the same or different independently represent a linear, branched or cyclic, saturated or unsaturated C_{1-24} alkyl radical or a C_{5-20}

aryl radical and wherein said radicals may optionally be substituted with halogen (F, Cl, Br, I), hydroxy, C_{1-4} alkoxy, C_{1-4}-alkyl, nitro or cyano.

5. The use according to claim 1, 2 or 3 wherein the fumaric acid derivative is selected from one or more fumaric acid monoalkyl esters of the formula II



wherein

- R_1 represents a linear, branched or cyclic, saturated or unsaturated C_{1-24} alkyl radical or a C_{5-20} aryl radical;

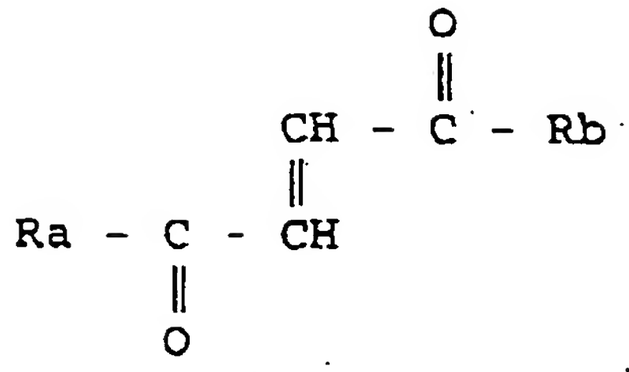
- A represents hydrogen, an alkaline or alkaline earth metal cation or a physiologically acceptable transition metal cation, preferably selected from Li^+, Na^+, K^+, Mg^{2+}, Ca^{2+}, Zn^{2+}, Fe^{2+}, and Mn^{2+}, and

- n equals 1 or 2 and corresponds to the valence of A.

6. The use according to any of the previous claims wherein the fumaric acid derivative is selected from one or more compounds of the formulae (I) and (II) and mixtures thereof.

7. The use according to claim 6 wherein the fumaric acid derivative is selected from the group consisting of fumaric acid dimethyl ester, fumaric acid diethyl ester, fumaric acid methyl ethyl ester, methyl hydrogen fumarate, ethyl hydrogen fumarate, calcium methyl fumarate, calcium ethyl fumarate, magnesium methyl fumarate, magnesium ethyl fumarate, zinc methyl fumarate, zinc ethyl fumarate, iron methyl fumarate, iron ethyl fumarate and mixtures thereof.

8. The use according to claim 1, 2, or 3 wherein the fumaric acid derivative is selected from one or more fumaric acid amides of the general formula III



(III)

wherein

R_a represents OR_3 or a D- or L-amino acid radical -NH-CHR_4-COOH bonded via an amide bond, wherein R_3 is hydrogen, a straight-chain or branched, optionally substituted C_{1-24} alkyl radical, a phenyl radical or a C_{6-10} aralkyl radical and R_4 is a side chain of a natural or synthetic amino acid; and

R_b represents a D- or L-amino acid radical -NH-CHR_5-COOH bonded via an amide bond, wherein R_5 is a side chain of a natural or synthetic amino acid which may be the same as or different from R_4, or a peptide radical with 2 to 100 amino acids bonded via an amide bond, which amino acids may be the same or different.

9. The use according to claim 8, wherein the side chain of a natural or synthetic amino acid is selected from the group consisting of the side chains of Ala, Val, Leu, Ile, Trp, Phe, Met, Tyr, Thr, Cys, Asn, Gln, Asp, Glu, Lys, Arg, His, Citrulline, Hcy, Hse, Hyp, Hyl, Orn, Sar, and Me-Gly, preferably Gly, Ala, Val, Ile, Leu, and Me-Gly.

10. The use according to claim 8 wherein R_a is the radical -OR_3 and R_b is an L-amino acid radical -NH-CHR_5-COOH or a peptide radical, R_5 being as defined in claim 8.

11. The use according to claim 1, 2, or 3 wherein the fumaric acid derivative is a carbocyclic oligomer consisting of 2 to 10 fumaric acid moieties as repetitive moieties, wherein the fumaric acid moieties are derived from monomers selected from the group consisting of fumaric acid, dialkyl fumarates, monoalkyl hydrogen fumarates, fumaric acid monoamides, fumaric acid diamides, monoalkyl monoamido fumarates and salts and mixtures thereof.

12. The use according to any of the previous claims wherein the alkyl radicals having 1 to 24 carbon atoms are selected from the group consisting of methyl, ethyl, n-propyl, isopropyl, n-butyl, sec-butyl, t-butyl, pentyl, cyclopentyl, 2-ethyl hexyl, hexyl, cyclohexyl, heptyl, cycloheptyl, octyl, vinyl, allyl, 2-hydroxy ethyl, 2 or 3 hydroxy propyl, 2,3-dihydroxypropyl, 2-methoxy ethyl, methoxy methyl, 2-methoxy propyl, 3-methoxy propyl or 2,3-dimethoxy propyl, preferably methyl or ethyl.

13. The use according to any of the previous claims wherein the drug is provided in a form suitable for oral, rectal, transdermal, dermal, ophthalmological, nasal, pulmonary or parenteral application.

14. The use according to claim 13 wherein the drug is provided in the form of tablets, coated tablets, capsules, granulate, solutions for drinking, liposomes, nano-particles, nano-capsules, micro-capsules, micro-tablets, pellets or powders and in the form of granules filled in capsules or sachets, micro-tablets filled in capsules or sachets, pellets filled in capsules or sachets, nano-particles filled in capsules or sachets or powder filled in capsules or sachets.

15. The use according to claim 14, wherein the drug is present in the form of nano-particles, pellets or micro-tablets which may optionally be filled in sachets or capsules.

16. The use according to any of the claims 14 to 15 wherein the solid oral dosage forms are provided with an enteric coating.

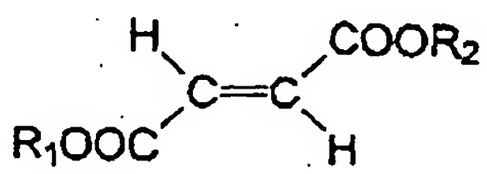
17. The use according to any of the previous claims wherein the drug contains an amount of fumaric acid derivative(s) corresponding to 1 to 500 mg of fumaric acid.

18. A method of inhibiting PDGF induced thymidine uptake of bronchial smooth muscle cells, which method includes the step of cultivating the cells in presence of an amount of a fumaric acid derivative sufficient to inhibit said uptake, which fumaric acid derivative is selected from the group consisting of dialkyl fumarates, monoalkyl hydrogen fumarates, fumaric acid monoalkyl ester salts, fumaric acid monoamides, monoamido fumaric acid salts, fumaric acid diamides, monoalkyl

monoamido fumarates, carbocyclic and oxacarbocyclic oligomers of these compounds and mixtures of the foregoing.

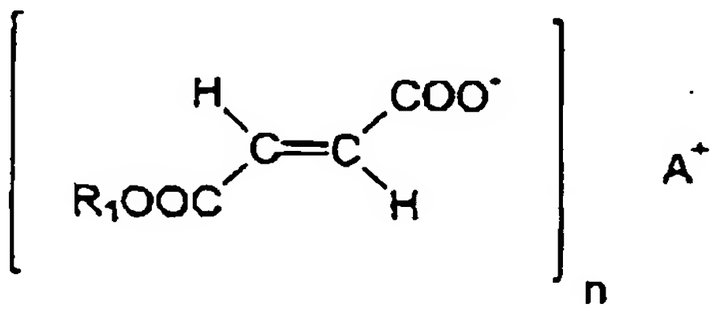
19. A method of inhibiting bronchial smooth muscle cell proliferation, which method includes the step of bringing bronchial smooth muscle cells directly or indirectly in contact with a proliferation inhibiting amount of a fumaric acid derivative selected from the group consisting of dialkyl fumarates, monoalkyl hydrogen fumarates, fumaric acid monoalkyl ester salts, fumaric acid monoamides, monoamido fumaric acid salts, fumaric acid diamides, monoalkyl monoamido fumarates, carbocyclic and oxacarbocyclic oligomers of these compounds and mixtures of the foregoing.

20. The method of claim 18 or 19, wherein the fumaric acid derivative is selected from one or more fumaric acid dialkyl esters of the formula I



wherein R_1 and R_2 which may be the same or different independently represent a linear, branched or cyclic, saturated or unsaturated C_{1-24} alkyl radical or a C_{5-20} aryl radical and wherein said radicals may optionally be substituted with halogen (F, Cl, Br, I), hydroxy, C_{1-4} alkoxy, C_{1-4}-alkyl, nitro or cyano.

21. The method of claim 18 or 19, wherein the fumaric acid derivative is selected from one or more fumaric acid monoalkyl esters of the formula II



wherein

- R_1 represents a linear, branched or cyclic, saturated or unsaturated C_{1-24} alkyl radical or a C_{5-20} aryl radical;

- A represents hydrogen, an alkaline or alkaline earth metal cation or a physiologically acceptable transition metal cation, preferably selected from Li^+, Na^+, K^+, Mg^{2+}, Ca^{2+}, Zn^{2+}, Fe^{2+}, and Mn^{2+}, and

- n equals 1 or 2 and corresponds to the valence of A.

22. The method of any of claims 21 or 22, wherein the fumaric acid derivative is selected from one or more compounds of the formulae (I) and (II) and mixtures thereof.

23. The method of claim 19, which is carried out in vivo, by administering the fumaric acid derivative to a subject.

24. The method of claim 23, wherein said administration is an oral administration.

25. The use of a fumaric acid derivative selected from the group consisting of dialkyl fumarates, monoalkyl hydrogen fumarates, fumaric acid monoalkyl ester salts, fumaric acid monoamides, monoamido fumaric acid salts, fumaric acid diamides, monoalkyl monoamido fumarates, carbocyclic and oxacarbocyclic oligomers of these compounds and mixtures of the foregoing, for inhibiting bronchial smooth muscle cell proliferation.

26. The use of a fumaric acid derivative selected from the group consisting of dialkyl fumarates, monoalkyl hydrogen fumarates, fumaric acid monoalkyl ester salts, fumaric acid monoamides, monoamido fumaric acid salts, fumaric acid diamides, monoalkyl monoamido fumarates, carbocyclic and oxacarbocyclic oligomers of these compounds and mixtures of the foregoing, for inhibiting PDGF induced STAT1 activation.